Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	3191	(fluorescence ADJ polarization) AND (bind$ OR inhibit$)	US-PGPUB; USPAT	OR	OFF	2005/10/20 13:47
S2	3380	(fluorescence ADJ polarization)	US-PGPUB; USPAT	OR	OFF	2005/10/20 13:48
S3	285479	(inhibition OR inhibitor)	US-PGPUB; USPAT	OR	ON	2005/10/20 13:48
S4	2421	S3 and S2	US-PGPUB; USPAT	OR	ON	2005/10/20 13:50
S5	740	S4 AND ((multiple OR many OR several) WITH (ligand OR inhibitor))	US-PGPUB; USPAT	OR	ON	2005/10/20 13:53
S6	83	S5 and @py<"2002"	US-PGPUB; USPAT	OR	ON	2005/10/20 15:08
S7	1	"5248791".PN.	USPAT; USOCR	OR	OFF	2005/10/20 14:51
S8	9	"5710129"	US-PGPUB; USPAT	OR	ON	2005/10/20 15:08
S9	980	oregon green	US-PGPUB; USPAT	ADJ	ON	2005/10/24 10:38
S10	15	S9 AND @py<="2000"	US-PGPUB; USPAT	ADJ	ON	2005/10/24 10:41
S11	44	difluorofluorescein	US-PGPUB; USPAT	ADJ	ON	2005/10/24 10:41

FILE 'CAPLUS' ENTERED AT 15:42:55 ON 24 OCT 2005
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FILE 'EMBASE' ENTERED AT 15:42:55 ON 24 OCT 2005

FILE 'MEDLINE' ENTERED AT 15:42:55 ON 24 OCT 2005
=> s fluorescence (2A) polarization (P) (inhibitor OR inhibition)
L4 1033 FLUORESCENCE (2A) POLARIZATION (P) (INHIBITOR OR INHIBITION)
=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 501 DUP REM L4 (532 DUPLICATES REMOVED)
=> s l5 AND (several OR many OR multiple)
L6 80 L5 AND (SEVERAL OR MANY OR MULTIPLE)
=> d ibib abs 1-10
=> s l6 and 2000/py
L7 4 L6 AND 2000/PY
=> s l6 and 1999/py
L8 4 L6 AND 1999/PY
=> s l6 and 1998/py
L9 2 L6 AND 1998/PY
=> s l6 and 1997/py
L10 4 L6 AND 1997/PY
=> s l6 and 2001/py
L11 3 L6 AND 2001/PY
=> s l7 or l8 or l9 or l10 or l11
L12 16 L7 OR L8 OR L9 OR L10 OR L11
=> d ibib abs 1-4
L12 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:319610 CAPLUS
DOCUMENT NUMBER: 133:187535
TITLE: Development of high throughput screening assays using fluorescence polarization: nuclear receptor-ligand-binding and kinase/phosphatase assays

AUTHOR(S): Parker, Gregory J.; Law, Tong Lin; Lenoch, Francis J.; Bolger, Randall E.

CORPORATE SOURCE: PanVera Corporation, Madison, WI, USA

SOURCE: Journal of Biomolecular Screening (2000), 5(2), 77-88
CODEN: JBISF3; ISSN: 1087-0571

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fluorescence polarization (FP) was used to develop high throughput screening (HTS) assays for nuclear receptor-ligand displacement and kinase inhibition. FP is a soln.-based, homogeneous technique requiring no immobilization or sepn. of reaction components. The FP-based estrogen receptor (ER) assay is based on the competition of fluorescein-labeled estradiol and estrogen-like compds. for binding to ER. These studies detd. the Kd for this interaction to be 3 nM for ERα and 2 nM for ERβ; IC50 values for 17β-estradiol, tamoxifen, 4-OH-tamoxifen, and diethylstilbestrol were detd. to be 5.6, 189, 26, and 3.5 nM, resp. In a screen of 50 lead compds. from a transcriptional activation screen, 21 compds. had IC50 values below 10 μM, with 1 having an almost 100-fold higher affinity for ERβ over ERα. These data show that an FP-based competitive binding assay can be used to screen diverse compds. with a broad range of binding affinities for ERs. The FP-based protein-tyrosine kinase (PTK) assay uses fluorescein-labeled phosphopeptides bound to anti-phosphotyrosine antibodies. Phosphopeptides generated by a kinase compete for this binding. In c-Src kinase reactions, polarization decreased with time as reaction products displaced the fluorescein-labeled phosphopeptide from the anti-phosphotyrosine antibodies. The exptl. detd. IC50 of AG 1478 was 400 pM, while genistein did not inhibit the epidermal growth factor receptor at similar concns. Like the FP-based PTK assay, the protein kinase C (PKC) assay utilizes competition. PKC isoforms had different turnover rates for the peptide substrate. The IC50 for staurosporine was < 10 nM for all PKC isoforms. Tyr phosphatase assays use direct binding rather than competition. Increasing concns. of T-cell protein-Tyr phosphatase (TC PTP) increased the rate of dephosphorylation. This change in polarization was dependent on TC PTP and was inhibited by 50 μM Na3VO4. The IC50 of Na3VO4 was 4 nM for TC PTP. These data demonstrate that a FP-based assay can detect

kinase and phosphatase activity. Homogeneous, fluorescent techniques such as FP are now methods of choice for screening many types of drug targets. New HTS instrumentation and assay methods like these make FP a technol. easily incorporated into HTS.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:209094 CAPLUS

DOCUMENT NUMBER: 133:72574

TITLE: Fluoresceinated FKBP12 ligands for a high-throughput fluorescence polarization assay

AUTHOR(S): Dubowchik, Gene M.; Ditta, Jonathan L.; Herbst, John J.; Bollini, Sagarika; Vinitsky, Alexander

CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492-7660, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(6), 559-562
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several fluoresceinated FKBP12 ligands have been prepd. for a high-throughput fluorescence polarization assay. Kis for FKBP12 rotamase inhibition by these ligands range from 1.3 μM to 32 nM, and their design is based on x-ray crystal structures of FKBP12 complexed with known immunophilin ligands.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs 5-8

L12 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:87598 CAPLUS

DOCUMENT NUMBER: 132:275788

TITLE: Detection of Phosphopeptides by Fluorescence

Polarization in the Presence of Cationic Polyamino Acids: Application to Kinase Assays

AUTHOR(S): Coffin, Jill; Latev, Maria; Bi, Xiahui; Nikiforov, Theo T.

CORPORATE SOURCE: Caliper Technologies Corp., Mountain View, CA, 94043, USA

SOURCE: Analytical Biochemistry (2000), 278(2), 206-212
CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have studied the interaction of several phosphopeptides with cationic polyamino acids such as polyarginine and polylysine by fluorescence polarization. The phosphopeptides used were labeled with fluorescein, and their net charges at the exptl. pH of 7.5 were 0, -1, -2, and -3. These phosphopeptides represent the products of enzymic phosphorylation reactions of the corresponding non-phosphorylated precursors by the protein kinase A, Akt1 (protein kinase Bα), and protein kinase C. We found that these phosphopeptides bind more strongly to the cationic polyamino acids studied than their non-phosphorylated analogs. This preferential binding of the phosphorylated peptides could be conveniently detected by an increase in the fluorescence polarization signal of the attached fluorescein residue. We have exploited this observation to develop a new approach for the detection of kinase activity that does not require radioactivity or sepn. of substrate from product. We have successfully used this method to perform Km detns. of the kinase enzymes for their substrates and Ki detns. of one of their inhibitors. This method for measuring kinase activity might be particularly useful for high-throughput screening applications. (c) 2000 Academic Press.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:711908 CAPLUS

DOCUMENT NUMBER: 132:44411

TITLE: Analysis of protein-peptide interaction by a

miniaturized fluorescence polarization assay using cyclin-dependent kinase 2/cyclin E as a model system

AUTHOR(S): Pin, Sokhom S.; Kariv, Ilona; Graciani, Nilsa R.; Oldenburg, Kevin R.

CORPORATE SOURCE: Leads Discovery, DuPont Pharmaceuticals, Experimental Station, Wilmington, DE, 19880-0400, USA

SOURCE: Analytical Biochemistry (1999), 275(2), 156-161
CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB As a result of the increasing size of chem. libraries, more rapid and highly sensitive strategies are needed to accelerate the process of drug discovery without increasing the cost. One means of accomplishing this is to miniaturize the assays that enter high-throughput screening (HTS). Miniaturization requires an assay design that has few steps, has a large degree of sepn. between the signal and background, and has a low well to well signal variation. Fluorescence polarization (FP) is an assay type that, in many cases, meets all of the above requirements. FP is a homogeneous method that allows interactions between mols. to be measured directly in soln. This article demonstrates the application of FP in a miniaturized HTS format, using 1536-well plates, to measure direct binding between cyclin-dependent kinase 2/cyclin E complex (CDK2/E) and an 8-mer-peptide kinase inhibitor. The data indicate that low variability and high specificity allow rapid and precise identification of antagonist compds. affecting CDK2/E-peptide interactions. (c) 1999 Academic Press.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs 9-12

L12 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:296437 CAPLUS

DOCUMENT NUMBER: 129:64503

TITLE: Selective inhibition of Ras interaction with its particular effector by synthetic peptides corresponding to the Ras effector region

AUTHOR(S): Ohnishi, Masako; Yamawaki-Kataoka, Yuriko; Kariya, Ken-Ichi; Tamada, Masako; Hu, Chang-Deng; Kataoka, Tohru

CORPORATE SOURCE: Department of Physiology II, Kobe University School of Medicine, Kobe, 650, Japan

SOURCE: Journal of Biological Chemistry (1998), 273(17), 10210-10215
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ras proteins possess multiple downstream effectors of distinct structures. We and others demonstrated that Ha-Ras carrying certain effector region mutations could interact differentially with its effectors, implying that significant differences exist in their Ras recognition mechanisms. Here, by employing the fluorescence polarization method, we measured the activity of effector region synthetic peptides bearing various amino acid substitutions to inhibit assocn. of Ras with the effectors human Raf-1 and Schizosaccharomyces pombe Byr2. The effect of these peptides on assocn. with another effector Saccharomyces cerevisiae adenylyl cyclase was also examd. by measuring inhibition of the Ras-dependent adenylyl cyclase activity. The peptide corresponding to the residues 17-44 competitively inhibited Ras assocn. with all the three effectors at the Ki values of 1~10 μM, and the inhibition was considerably attenuated by the D38A mutation. The peptide with the D38N mutation inhibited assocn. of Ha-Ras with Byr2 but not with the others, whereas that with the P34G mutation inhibited assocn. of Ha-Ras with Raf-1 and Byr2 but not with adenylyl cyclase. Thus, the specificity obsd. with the whole Ras protein was retained in the effector region peptide. These results suggest that the effector region residues constitute a major determinant for differential recognition of the effector mols., raising a possibility for selective inhibition of a particular Ras function.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT